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A MODERN CONCEPTION OF THE ACTION OF THE NERVOUS SYSTEM[1]

By Professor G. H. PARKER

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IT was my privilege as a young student of zoology to have made the acquaintance of Professor W. K. Brooks in the summer of 1889 at the Laboratory of the United States Fish Commission, Woods Hole. Here a body of mature investigators in marine biology was gathered and we younger workers were allowed to associate with them greatly to our advantage. It is an honor to be invited by Miss Fowler to deliver this lecture, and it would be a pleasure to me if I could think of it as a small return to Dr. Brooks for the kindly help and encouragement he gave to all of us who were associated with him at the Woods Hole Station. In a way this lecture is an appropriate tribute to Dr. Brooks, for much of its contents was brought to light in those laboratories that have grown up at Woods Hole around the original one where he worked. I am further disposed to think that the special subject herein discussed, the mode of interaction of nervous elements, would have claimed a fair share of Dr. Brooks's interest, for his philosophical temperament would have led him not only to seek a clear picture of the nervous mechanism in animals, but to gain an insight into the way in which this mechanism acts.

The histologists of half a century ago described the nervous system as composed of ganglion-cells, nerve-fibers and fibrillar material. With the advent of the Golgi method in the last quarter of the past century it became possible to determine the relations of these

[1] Third William Keith Brooks Lecture, delivered at Greensboro College, Greensboro, N. C., April 25, 1940.

elements to each other. Golgi's idea that the fibrillar material forms a true network was abandoned for Ramòn-y-Cajal's conception of the fibrillar substance as a system of branches by which one nerve-cell is brought into contact with others but without real unions. This separateness of the nerve-cells was foreshadowed in the embryological studies of His and was abundantly confirmed subsequently by the histogenetic investigations of Harrison.* Meanwhile Waldeyer in 1891 had seized upon this revised histological picture of the nervous system, and, recognizing that nerve-fibers were parts of nerve-cells, had been led to the conception of the true histological units or neurones whose functional continuity was through fibrillar contacts. These points of mutual contact, the synapses, were shown by Sherrington to have a kind of transmission unlike that of a nerve-fiber. They proved to be polarized in that they transmitted nerve impulses in one direction only as contrasted with the double conduction in nerve-fibers. Synaptic transmission moreover was more time-consuming than fiber transmission. Many neurophysiologists have interpreted synaptic transmission as a purely electrical phenomenon, but of recent years there has been a growing opinion that synaptic transmission is accomplished by substances, variously designated as neurohumors, neurohormones, or chemical activators, which, produced on one side of the synapse, pass across the minute interruption and stimulate the opposite side. The chief question to be discussed in this lecture is whether there is evidence for the existence of such substances and what their natures may possibly be.

Such substances may be sought between receptor-cells and their associated nerve-fibers, or where one neurone is in contact with another in nervous organs, or finally where efferent neurones terminate on effectors such as muscles, glands, color cells and the like. It is to the last set of these contacts, those between chromatic nerve-fibers and their associated color cells or chromatophores that I propose to direct your attention.

By means of chromatophores lodged for the most part in the skins of many animals these creatures can change their color in many directions and often with astounding quickness. These changes were well known to the ancients and were recorded by Aristotle and by Pliny. They have excited the attention of naturalists down the ages. Such changes are to be seen among squids and devil-fishes, shrimps and prawns, and among the lower vertebrates including the fishes, the amphibians, and the lizards. Incidentally many other animals show such changes, but the best-known examples are found among the groups just indicated. For conciseness I shall limit my discussion to the chromatic activities of the lower vertebrates.

If a smooth dogfish, Mustelus, be placed in an illuminated marine aquarium with white sides and white bottom, it will assume in the course of a few days a pale, translucent flesh-tint. Placed now in a similar black-walled tank, it will become in a day or so deep gray. These color changes from dark to pale and the reverse constitute the whole color range of this fish and are accomplished by the concentration or dispersion of a dark pigment, melanin, in myriads of chromatophores in the skin of this fish. In the concentrated state the chromatophores or, better, melanophores are black dots each about 30 microns in diameter; in the dispersed state they are richly branched, dark bodies each covering an area roughly 200 microns in diameter. As dots they are inconspicuous in the total area of the skin and induce the pale tint in the fish, but as branched bodies they together cover large areas of skin and bring about the dark coloration. This relatively simple mechanism illustrates the device by which most lower vertebrates change their tints though in many of these animals their melanophores are supplemented by chromatophores of other colors, red, orange, yellow, white, and the like.

In 1858 the celebrated English physician Lister studied the color changes of the common frog and made the discovery that the integrity of the eyes in this animal was necessary for its chromatic activities. He concluded that these activities were in the nature of nervous reflexes and were mediated by the central nervous system of the animal. Pouchet, in a series of papers published between 1872 and 1876, showed that in fishes the parts of the nervous system especially concerned with color changes were the sympathetic or autonomic tracts. In the first quarter of this century Sumner and subsequently Mast demonstrated that certain fishes, the flatfishes or flounders, not only changed their general tint but also modified their color patterns to fit in a rough way that of their surroundings. This change of pattern may be regarded as perhaps the most complicated of the color changes in any animal and represents in this respect the pinnacle of efficiency in such chromatic systems.

Up to about 1920 all investigators in this field of research accepted the nervous interpretation of the control of animal color changes, but beginning with 1922 a novel view concerning such changes was advanced. In that year Hogben and Winton showed by a variety of tests that the nerves in frogs had little or nothing to do with the color changes in these animals, but that such changes were dependent upon an internal secretion from the pituitary gland. A frog from which this gland had been removed became pale and remained so. On injecting into such a pale animal an extract of the intermediate lobe of this gland it was observed that the creature became very dark but blanched again after time had been given for the extract to have disappeared. From this and other like

tests Hogben concluded that amphibians became pale when the pituitary secretion, now called intermedin, was absent from their blood and that they were dark when this substance was present in their circulation. He was thus led to contrast the hormonal control of color changes in amphibians with the nervous control of these changes in the fishes and in the lizards. Hence so far as the color changes of amphibians were concerned an entirely novel element was introduced. To discuss the importance of hormonal or humoral agents in color changes I propose to consider the chromatic activities in three lower vertebrates, the frog, the smooth dogfish, and the catfish.

The chromatic system in the frog so far as activation is concerned may well represent the simplest type of this process. As I have already mentioned, Hogben and Winton expressed the view that the color changes in the frog were fully explicable from the standpoint of the presence or absence of a single chromatic secretion. This opinion was espoused by Parker and Scatterty. Meanwhile Hogben and Slome in their study of the South African toad Xenopus were led to conclude that amphibians possessed a second and in this instance a blanching neurohumor also from the pituitary gland, a conclusion supported by the work of Soderwall and Steggerda on frogs. Whether amphibians possess one, two or more chromatic hormones is an open question, but however this may be, it is agreed by all recent physiological workers that melanophore activation in the frog is humoral and not nervous. The innervation of frog melanophores as shown in histological preparations by some recent students of this subject (Perotti, Tusques) has in no instance been demonstrated to be concerned with color changes and may well have to do with other nervous functions. A purely humoral activation of chromatophores appears to hold not only for amphibians, but also for the lamprey eels (Young), most sharks and rays (Young, Parker, Wykes), the Carolina lizard (Kleinholz), and the shrimps, prawns, crabs and the like (Perkins, Koller, Abramowitz, Hanström, Carlson, Brown, Kleinholz and others).

A second type of chromatic activation is to be seen in the smooth dogfish Mustelus. Like the frog this fish becomes pale on the loss of its pituitary gland and darkens again temporarily to an injection of pituitary extract (Lundstrom and Bard). When its cutaneous nerves are cut the denervated areas become pale, and the electric stimulation of cutaneous nerves also induces local blanching. Hence in Mustelus active blanching is nervous though favored by the absence of intermedin. In this fish then darkening is due to intermedin and blanching is the result of the action of concentrating nerves (Parker and Porter). Blanching in Mustelus, suspected of being caused by vasomotor changes (Hogben, Wykes), has been shown to be independent of circulatory disturbances (Parker). Another chromatic vertebrate which appears to have a combined system partly humoral and partly nervous is the horned toad (Phrynosoma), a lizard of the North American deserts. As a matter of fact the chromatophoral system in this creature resembles in a striking way that in Mustelus, for the darkening of Phrynosoma is due to intermedin and its blanching is the result of the action of concentrating nerves (Redfield, Parker).

The third example of color change to which I wish to call your attention is that of the catfish Ameiurus. This fish has a melanophore system which enables it to range from a very pale greenish yellow to coal-black. Its dark phase is dependent chiefly upon intermedin from its pituitary gland. If in a pale fish one of its radiating caudal nerves is cut, a dark band corresponding to the area of distribution of the nerve will form. This type of response has long been known in other chromatic vertebrates and has been commonly attributed to paralysis. If, however, a pale fish in which such a caudal band has been formed is kept in a white-walled illuminated aquarium, the band will blanch in a few days. If now the nerve is cut a second time and at a point a little distal to the first cut, a second band will form and remain conspicuous for a day or two. The formation of this second band shows that the production of such bands can not be due to paralysis, for the nerve to form this renewed band must be still active. The nerve is without doubt reactivated by the second cut, and the particular fibers thus brought into action are dispersing fibers. This test and others like it have led to the conclusion that Ameiurus darkens not only through the action of intermedin but also by means of dispersing nerves. Ameiurus blanches in consequence of concentrating nerves whose action in this and many other fishes has long since been demonstrated by electric stimulation. Thus the melanophores of Ameiurus have a double innervation, one set of nerve-fibers controlling the dispersion of pigment and the other the concentration of this material. Such a double innervation is consistent with the histological discoveries of Eberth, Ballowitz, and Eberth and Bunge all of whom have shown that two or more nerve-fibers may reach the same melanophore. The double innervation of teleost melanophores has also been demonstrated in studies of partly innervated areas and in the regeneration of melanophore nerves (Mills, Parker and Porter, Abramowitz). The catfish then represents what may be regarded as an extreme instance in chromatic complication in that its color system involves concentrating and dispersing nerve-fibers and intermedin. This complex system has been shown to occur in a number of other teleosts, and

it is probably present in the African chameleon. Thus from the frog with its possible single chromatic humor, intermedin, one may pass to mixed chromatic systems with one set of nerve-fibers and intermedin, as in Mustelus, or to those with two sets of fibers and intermedin, as in Ameiurus. No chromatic vertebrate is known that does not possess intermedin as a darkening agent, though in some, as for instance Fundulus, this agent may be very subordinate. Mixed systems, partly humoral and partly nervous, occur among fishes and lizards. Apparently there is no instance in the vertebrates of a purely nervous chromatic system.

What are the details of melanophore activation? Of the agents to this end intermedin is the most obvious and universal in the vertebrates. Under appropriate environmental conditions this substance is discharged from the pituitary gland of a given chromatic animal into its blood by which the intermedin is carried over the animal's body to its melanophores. These cells are thereby excited to disperse their pigment. Thus intermedin appears to act directly and immediately on the color cells themselves. The way in which the chromatic nerves, dispersing and concentrating, influence melanophores can be surmised best by studying the blanching of dark bands in the tails of such forms as the killifish and the catfish.

A dark band produced in the tail of a pale killifish or a pale catfish by cutting a bundle of chromatic nerve-fibers will blanch in such a fish on a white background in one or more days. Such a band does not blanch uniformly but begins to fade first on its edges leaving its axis dark. Finally the dark axis fades completely. In the killifish bands one millimeter wide blanch on the average in about 30 hours, those two millimeters wide, in some 78 hours (Parker). In a catfish a band one ray in width becomes pale in 2 days, one two rays wide in 5 days and one three rays wide in 10 days (Abramowitz). These peculiarities show that the fading band is not influenced uniformly as, for instance, from below by the blood and lymph, but that it is changed by something that affects it laterally. Either a substance escapes from the sides of the band and by its absence allows the lateral melanophores to concentrate their pigment or an external agent makes its way from the surrounding tissue into the edges of the band and thus induces pigment concentration. Matsushita has performed an experiment which shows that the second of these alternatives is the correct one. If a new caudal band is cut in a pale fish and in such a position that on one of its sides there is a fully blanched denervated band and on the other the normal innervated pale area of the tail, its method of fading will be significant. Matsushita showed that it fades only on that side which is next the innervated pale area and not on the opposite denervated side. Its blanching is therefore not due to the loss of a darkening substance, for this could escape equally from either side. It must result from the invasion of a blanching agent whose source is the innervated pale portion of the tail. In a somewhat similar way it has been shown that a denervated pale band will darken over only that portion of its extent which is flanked by two newly formed dark bands of half the length of the pale band and not over that part not so flanked (Parker). Thus there is good reason to conclude that pale innervated regions contain an active concentrating substance and that dark nervously active regions contain an equally effective dispersing substance. Both these substances may pass by slow degrees from their regions of origin into adjacent regions. Since the regions of origin of the concentrating substance are the regions of active concentrating nerve-fibers and the regions of origin of the dispersing substance are the regions of activated dispersing fibers, it is natural to conclude that these substances are the products of their respective sets of nerve-fibers each in its particular way activating the melanophores concerned.

It has already been pointed out that these substances do not act as though they were dissolved in blood or in lymph. They are much too circumscribed in their effects and much too slow in their spread to be in aqueous solution. The only other constituents of the tissues in which they are likely to be dissolved are the lipoids, and it is probable that these activating substances are carried in such fatty materials and that they migrate by diffusing slowly through such materials. This view is supported by the fact that an Italian olive-oil extract of a dark catfish skin when injected as a coarse emulsion under the skin of a pale catfish will cause the formation of areas of dark color. These dark areas can not be produced by injections of pure olive oil or by oil extracts of tissues of other than dark skin. They are therefore believed to be due to some substance dissolved from the dark skin by the oil. Such oil-soluble materials have been called lipohumors in contrast to hydrohumors like, for instance, intermedin which, as already indicated, act in aqueous solution on melanophores (Parker).

Although the dispersing and the concentrating lipohumors of the catfish give evidence of being normally dissolved in the lipoid constituents of its skin, these humors appear to be also soluble in water. Dissolved in this medium they may be tested for their chemical characteristics. Aqueous extracts of the dark skins of catfishes when appropriately prepared and applied to the muscle of the leech give every evidence of containing acetylcholine. This substance moreover when injected into a catfish previously treated with eserine will darken the fish. It is therefore probable that the darkening lipohumor of the catfish is acetylcholine (Chin; Chang, Haieh, and Lu; Parker). This sub-

stance has long been known to be a most remarkably efficient agent in many organic operations, and this peculiarity appears in the darkening of the catfish, for the skin of this creature is of a deep hue when it contains one part by weight of acetylcholine to about 13,000,000 parts of skin.

If it is probable that the dispersing nerve-fibers of the catfish act on melanophores through the neurohumor acetylcholine, what can be said of the concentrating fibers? Here aqueous solutions may also be used in tests. When such solutions properly prepared are applied to the frog's heart they are found to give evidence of containing adrenaline (Parker). As has long been known this substance when injected directly into a dark catfish will cause it to blanch. Hence there is reason to believe that just as the dispersing nerve-fibers probably act on melanophores through the production of acetylcholine, so the concentrating fibers affect melanophores by the discharge of adrenaline. This substance, though a highly efficient agent in the control of organic activities, is by no means so remarkable in this respect as acetylcholine. A catfish will blanch when its skin contains one part by weight of adrenaline in 350,000 parts of skin. Thus in the catfish the concentrating fibers appear to produce adrenaline and may be classed therefore as adrenergic; and the dispersing fibers acetylcholine and hence classed as cholinergic.

The nervous component of the melanophore system in the catfish is therefore organized upon the plan of opposing sets of nerve-fibers with their appropriate neurohumors as occurs in other parts of the autonomic system. But the melanophore system in this fish has in addition to these two neurohumors a third one, intermedin, which, so far as is known, has not been identified in other parts of the nervous organization of vertebrates. Nor is this the limit, for the chromatophore system in other fishes includes in addition to melanophores other types of color cells such as xanthophores, erythrophores, leucophores and the like, none of whose activities has been so fully analyzed as those of the melanophores, yet whose functional performances are such as to imply the presence of other and different neurohumors. Thus the conditions in chromatic vertebrates give promise of a considerable array of these substances still to be discovered.

But more important than a promised increase in the number of neurohumors is the peculiar behavior of the two nervous components in the catfish to their organic environment. Acetylcholine when introduced in aqueous solution into the body of a catfish is quickly destroyed by the cholinesterase of the animal's tissues. If, however, it is introduced dissolved in oil, it will remain effective for days. Apparently it is protected from such agents as cholinesterase by being in solution in the oil and it only slowly and gradually diffuses out from this medium into the adjacent aqueous environment. Here it may act momentarily on the melanophores before it suffers destruction. Thus oily deposits in general, including the cell lipoids, may serve as protective reservoirs for acetylcholine and in consequence greatly lengthen the period of this agent's activity. In this way the darkening action of acetylcholine may be greatly prolonged.

The same seems to be true of adrenaline. Although this substance is not rendered ineffective in the fish's body with any approximation to the rapidity with which acetylcholine is, it is nevertheless none too stable and in oily mixtures its activity far outlasts in point of time that which it shows in purely aqueous solution. This feature of neurohumoral activity is not without general biological significance, for it points to lipoids and other like substances as possibly important protective repositories for susceptible agents whose existence in aqueous solution in the organism might be very limited and precarious.

From this brief survey of the means of activation of a limited group of chromatophores it must be evident that neurohumors not only exist in animals, but that they exist in reasonable variety. They may be defined as hormones produced by nervous tissue or by glands appended to that tissue and concerned with the activation or inhibition of other nervous tissue or its effectors. That they occur in many parts of the nervous system is beyond doubt; that they serve in certain regions as means of synaptic transmission is highly probable; but that they are the exclusive means of such transmission can not at present be affirmed. This uncertainty leaves open still the possibility of electrical transmission in certain places. It is, however, conceivable that even here neurohumoral transmission may also occur and that in such instances these two supposedly different types of transmission may be merely two aspects of the same operation (Forbes). In conclusion it may be said that neurohumoral transmission offers a natural explanation for synaptic polarization, for if one side of the synapse is secretory and the other receptive, transmission would naturally be in one direction only. Moreover such a double operation might well be expected to involve synaptic delay not to be looked for as a necessary step in electric transmission. Because of these features the neurohumoral rather than the electric conception of transmission at the synapse has been gaining ground and the general conception that complex nervous activity involves a myriad of momentary neurohumoral discharges and receptions is coming to be a significant picture in the minds of modern neurophysiologists (Dale).

ENGINEERING AND RELIGION[1]

By DUGALD C. JACKSON, JR.
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HIGHER education is primarily concerned with intellectual training and the acquisition of knowledge concerning existent facts. However, the importance of the development of the individual and his personality has come before engineering educators in more recent years. Much thought and discussion has been given to the fact that humanistic subjects (the so-called cultural subjects) have a part in the development of the student.

The early steps were merely the insertion of presumably beneficial humanistic subjects into the engineering curricula as separate and individual courses. Gradually there has come the recognition that there is need for an interrelation among these discrete humanistic subjects and that they should be an integral and coordinated part of the engineering curricula. Although the necessity for humanistic subjects in the engineering curricula is accepted, there is difference of opinion as to what proportion of an engineering curriculum should consist of humanistic subjects, and as to whether certain subjects should be included or omitted. In other words, the amount of humanistic subjects included in the engineering curricula, and the *extent* of their coordination and integration with these engineering curricula seems still to be much a matter of debate, but the *need* is an accepted fact. Generally speaking, the various opinions advanced on these matters are soundly based and entirely justified, provided full weight is given to the conditions of the individual engineering school where a particular method is being used.

In spite of all the thoroughgoing consideration that has been given to the all-around development of the individual engineering student and the many lengthy discussions that have been held concerning both the fundamental principles involved and also the detailed mechanisms for achieving the results, little attention seems to have been directed to determining whether the study of humanistic subjects provides a fundamental development of the individual student or whether it is somewhat of a superficial intellectual veneer. When we speak of the all-around development of a student, we may use the general and indefinite phrase that "we want to develop his personality." Because the term personality is so indefinite and may mean so many things to different people, we tend to throw this into the discard as being an undesirable term to use in dealing with engineers. Whether or not we are engineers, we rather generally are not satisfied in our discussions unless we define our terms—and personality is intangible and to most of us seems rather undefinable. Yet it has a very definite and strong meaning to all of us, a meaning that is closely related to the individual himself, his inward being, his innermost soul. And unless we can determine whether or how subjects of study affect a student's personality, we can not in any way be sure that they are broadening his view or developing him as a person who will be a useful citizen and a satisfactory member of society.

From a qualitative observation of graduates of engineering schools, it is evident that exposure to humanistic studies has some beneficial effect upon the development of a man's personality. There also appears to be evidence that the closer the coordination of the humanistic studies with the technical studies, and the more thoroughly the humanistic studies are integrated into the engineering curriculum, the greater and more beneficial will be the effect upon the individual student. Many reasons have been advanced to account for this desirable result. Probably all of them are in a large part correct, but probably all of them miss, in some degree, the vital point as to how the humanistic studies affect the inner man.

The personality of a student has been developing from its early days and has been influenced directly by his associates (family, friends, teachers), but through it all there is an influence that we as engineering educators seem inclined to overlook, if not actually to forget—the influence of religion. Religious faith is implanted in each individual as a small child, along with his first toddling steps or even earlier. Religious faith is one of the first things that mothers, either consciously or unconsciously, teach their children. It becomes ingrained in the person. It can not be overlooked. It has a direct and lasting effect on the development of the personality. Religious faith can be dampened until it is fairly non-existent, or it can be nurtured and cultivated into thoroughgoing convictions, based to a large extent upon reason.

Religious faith and religious conviction are an integral and essential part to each and all of us. They have been a stimulating force in the forwarding and developing of civilization through the ages. They must not, therefore, be forgotten or omitted in considering how best to develop the engineering student into full bloom in the engineering profession as a well-rounded and competent individual and a desirable member of society.

[1] Presented at the meeting of the Illinois-Indiana section, Society for the Promotion of Engineering Education, at the University of Notre Dame, April 20, 1940.

To my mind the education of an engineering student while in college may be considered as falling into three groups or channels: the acquisition of scientific and technical knowledge and training and ability to apply it, a broadening education of humanistic subjects, and the development of religious faith into substantially a reasoned religious conviction. It is a generally accepted practice in engineering schools to include the first two groups in their engineering curricula and to endeavor to bring them into a homogeneous entity, a sort of monolithic slab of engineering education with the humanistic subjects spreading among the scientific and technical subjects and impermeating them as the cement spreads throughout the sand and gravel and binds it together in a single structure. In non-denominational institutions, such as state universities, by our present American practices, religion may not be taught formally to all the students; the students must continue their education in religion on an individual, personal and informal basis with the religious organizations on the campus or with the churches in the vicinity. This makes it difficult, well-nigh impossible, to make their religious training an integral part of their formal education. At the same time their religious convictions are developing and are having strong influence—perhaps stronger than anything else—upon the development of their personality, which in turn will greatly affect their progress and achievement in later life. In my opinion there is strong argument for the taking of courses in religion during college education—courses that will make an intellectual approach upon religion and will aid the student in converting his unreasoned faith, which he has absorbed from parents and church, into a reasoned conviction. In institutions where courses in religion are offered, this result can be achieved by the student himself, but the greatest effectiveness can be accomplished if the religion courses, like the humanistic subjects, are brought into the engineering curricula as an integral and cognate part. The principles brought out in the courses of religion need to be utilized both in the humanistic subjects and in the technical subjects. Especially is this important in the upper class years when we, as engineering educators, are inculcating in our engineering students the ideals of the profession and the ideas of professional ethics.

At the University of Notre Dame, in addition to the requirement of courses in religion, the students have to take certain courses in philosophy. We are utilizing these philosophy subjects to aid us in coordinating the religious principles with the every-day life of the professional engineer. Philosophy may be considered as the bridge or tie between courses in religion and the technical subjects.

I feel that our objective in the engineering college at Notre Dame is to develop fine men who will be excellent citizens and first-rate engineers. I wish to quote from a discussion of the instruction in philosophy that Professor Roemer, of the Notre Dame philosophy department, has presented to me at my request:

> May I be allowed to submit that in this hectic struggle for existence while there is persistent demand for technicians in many fields of engineering, the engineer is apt to forget that before he is a professional man, he is first of all a *man*. If we who claim to be educators and builders of men forget that we are molding the minds and hearts of human beings who, like ourselves, have rights and duties in society, how can we expect our finished product to be complete?
>
> Apart from religious doctrine, there are the cultural disciplines to which an educated man must need have submitted before he can be credited with having developed his intellectual faculty to its maturity. Chief of these cultural disciplines are those of language and those of fundamental philosophy. Here, logic enters so that the future executive may know how to think straight. He should be made familiar with the inductive or scientific method and also something of the purely deductive method which finds exemplification in the philosophy of mind and in ethics.

Before closing I wish to read some excerpts from the report of the Society for the Promotion of Engineering Education, "Committee on Aims and Scope of Engineering Curricula." These excerpts indicate the increasing recognition of the need of dealing with social problems by the engineering profession in general and by the individual engineer.

> From its very nature, engineering education operates under changing conditions which constantly challenge its processes and test its results. Its recent history has therefore been one of continuing appraisal and adaptation to changing needs.
>
> Continuation of this process of self-examination seems now to be called for by new conditions, trends and attitudes that will be readily recognized: (a) The thoughtful public has become aware in recent years of the technological nature of our civilization and of the part that engineers must play in the solution of many of its problems. There is therefore a wide-spread insistence that the technological professions should be competent to evaluate the social problems with which they deal and to recognize the social forces which they create.
>
> There is among engineering colleges a basic uniformity of aims, ideals, methods and standards of undergraduate instruction. This homogeneity is not the result of any imposed standardization; it is derived from a strong sense of solidarity among the different institutions and from the common ends they serve. In these circumstances there is ample opportunity for well-considered variations in curricula and for educational experimentation. . . . Diversity is, in fact, one of the basic characteristics of engineering services.

Engineering education rests on a foundation of science, of humanities and of social relationships. . . .

First (proposed policy), broadening of the base of engineering education, now in process, should be continued. Its roots should extend more deeply into the social sciences and humanities as well as into the physical sciences in order to sustain a rounded educational growth which will continue into professional life. Two stems are thus implied in the undergraduate curriculum which we have designated as the scientific-technological and the humanistic-social.

The humanistic-social studies should be directed toward (six objectives, one of which is stated as): 5. Development of moral, ethical and social concepts essential to a satisfying personal philosophy, to a career consistent with the public welfare and to a sound professional attitude.

Undergraduate curricula should be made broader and more fundamental through increased emphasis on basic sciences and humanistic and social studies.

No measures taken with respect to engineering education should limit the freedom that now exists for experimentation and change.

Proper consideration of social problems can not be given nor adequate solutions made unless we use the engineering method of obtaining all information pertinent to the specific problem. We do not have all information unless we have an understanding of religious faith and convictions, and their effect upon the actions and viewpoint of individuals. Since the engineer, increasingly in the future, will be concerned with social, in addition to technical and economic problems, it is important for him to have knowledge of religious principles and their result and effect on the individual. This in turn places the charge upon us as engineering educators to determine how far the training in religious principles should be brought into engineering training as a formal part of the curricula. I submit that religious faith and some knowledge of religious principles is ingrained in our students, and for this reason, so far as practicable, definite attention to integrating an intellectual study of religious principles and convictions into the engineering curricula is desirable, if not actually essential, for the best progress of the profession of engineering in its broadening scope in approaching social relationship in the future.

SCIENTIFIC EVENTS

SCIENTIFIC AND TECHNICAL DEVELOPMENTS OF USE IN THE WAR

A SPECIAL cable from London has been received by *The New York Times* which reads:

The government has set up a scientific brain trust headed by Lord Hankey to give the scientific workers of Britain more scope in inventive prosecution of the war and in countering the enemy's arms. Acknowledged leaders of various branches of science, whose appointment to the new scientific advisory committee was announced to-night, will form a central clearing house for new ideas.

Among the men on the committee are Sir William Bragg, member of wartime committees on food and fuel; Dr. Edward Victor Appleton, radio expert, who was called in by the government before the war to improve civil defense against bombers; Professor Archibald Vivian Hill, one of the world's foremost physiologists and a leading authority on aerodynamics and anti-aircraft defense.

From the public point of view the most immediate problem facing the new body is perfection of a weapon against night bombers.

An important job of the committee is to see that no new scientific or technical developments go neglected. Members will examine original ideas and pick out those they think can be used or developed after experiment. The members also will bring their individual and combined gifts to the services of their country.

A correspondent of the London *Times* writes under date of September 2 that the Canadian Government has announced the appointment of a committee of nine members which will administer the funds presented to patriotic citizens for assisting important technical projects and scientific investigations now being undertaken or proposed by the National Research Council with the object of increasing the efficiency of the Canadian war effort.

The chairman of the committee is Dean C. J. Mackenzie, acting president of the National Council, and the members include Sir Frederick Banting, J. S. Duncan (Deputy Minister for Air), Professor Otto Maass, head of the department of physical chemistry of McGill University, and Colonel Allen Magee, executive assistant to the Minister of National Defense. It is understood that the funds given or promised amount to nearly $1,000,000. The committee is empowered to coopt donors to serve as non-voting members.

DEDICATION OF THE NATURAL RESOURCES BUILDING AT THE UNIVERSITY OF ILLINOIS

ON the occasion of the dedication of the new Natural Resources Building of the University of Illinois on November 14 and 15, the Illinois Geological Survey of the State Department of Registration and Education, the Engineering Experiment Station of the University of Illinois and the Illinois Mineral Industries Committee extend an invitation to all the mineral industries of Illinois and of other states, and to all allied organizations, to join them in holding a mineral industries conference.

The official announcement points out that the com-

pletion of the Natural Resources Building promises to begin a new chapter in the development of the state. It is equipped with the most modern facilities for research, with complete offices and laboratories, that will make it possible to pursue research investigations of the natural resources of Illinois that, although planned, until now have had to be postponed for want of adequate facilities.

The Mineral Industries Conference will begin with an open-house gathering on Thursday morning that will afford an opportunity for complete inspection of the new offices and laboratories of the Geological Survey. At noon there will be an all-mineral-industries luncheon followed in the afternoon by concurrent separate sessions on coal, oil and gas, clay and clay products, rock and rock products, and a symposium on "The Geology of the Devonian System" conducted jointly with the department of geology of the university. There will be a general mineral industries banquet on Thursday evening.

In honor of the dedication of the new building, the Industrial Minerals Division of the American Institute of Mining and Metallurgical Engineers will hold its autumn meeting in Urbana and its members will participate in the sessions on clay and rock products. The dedication ceremonies will take place on Friday afternoon under the auspices of the Board of Natural Resources and Conservation and the University Board of Trustees. Dr. Isaiah Bowman, president of the Johns Hopkins University, will give the dedication address.

The Natural History Survey, which shares the building with the Geological Survey, will also sponsor conferences for its allied groups, and they will join in the dedication. State officials will be present and also delegates from leading universities and research institutions of the country, and from various scientific and technical societies.

Following the ceremonies a reception will be held in the foyer of the Natural Resources Building and in the evening all groups will join in a dedication banquet.

NEW DISPENSARIES IN NEW YORK CITY

THE cornerstone laying ceremony at the Kings County Hospital, Brooklyn, N. Y., of the third of a series of ten new modern dispensaries, planned by the Department of Hospitals for different sections of the city, was held on September 25. The speakers were: F. H. La Guardia, mayor of the City of New York; John Cashmore, president of the Borough of Brooklyn; Irving V. A. Huie, commissioner of the Department of Public Works; Dr. Walter A. Coakley, president of the Medical Board; Dr. Emanuel Giddings, medical superintendent, and Rev. Charles E. Schmidt, chaplain. Dr. S. S. Goldwater, who has now retired as commissioner of the department of hospitals, presided.

The building for the dispensary, which will be erected at the cost of a million dollars, will be a five-story, steel-framed structure with concrete foundation and floors, and exterior walls of brick, trimmed with limestone with a granite base.

In a statement made by Dr. Goldwater he pointed out that legitimate demands for the services of the clinic by citizens unable to pay for private medical care continue to increase. As a sample of the increases that have been experienced at all the clinics, he said that at the Kings County Hospital clinic visits had increased from 163,638 in 1933, when the present quarters were first opened, to 358,072 in 1939. He said further:

> The additional space which the new dispensary makes available will greatly facilitate the registration of patients, thereby avoiding the necessity of long hours of standing in line. Provision will be made for registration of double the present number of patients treated daily. Examining rooms will be provided where physicians in light, bright surroundings, unencumbered by the stress of overcrowding, will be able to give better service to the patients. The tuberculosis clinic, now housed in makeshift quarters in the tuberculosis pavilion of Kings County Hospital, will occupy quarters in the new dispensary which will provide a complete set-up for fluoroscopy and collapse therapy. The expanded social service division of the dispensary will provide more privacy and a more cheerful atmosphere for the solution of the many problems of clinic patients. In addition, it will provide more space for the adequate follow-up of venereal, fracture and luetic prenatal cases. Extensive equipment for x-ray and physical therapy will be provided in the building, thus relieving the strain on departments originally intended for hospital service only.

In the development of the dispensaries first relief was sought at Greenpoint Hospital, also in Brooklyn, where a modern building was opened in 1937. The second dispensary in the series was the Welfare Island (Consolidated) Dispensary at East End Avenue and 80th Street, Manhattan, which was opened on August 1 of this year and which serves patients of the three city hospitals on Welfare Island. Other new dispensaries or major additions to present services for the relief of indigent patients have been authorized and planned at Queens General Hospital in Jamaica, Coney Island and Cumberland Hospitals in Brooklyn, Lincoln and Morrisania Hospitals in the Bronx, and Harlem and Bellevue Hospitals in Manhattan.

CENTENNIAL CELEBRATION OF THE COLLEGE OF MEDICINE OF NEW YORK UNIVERSITY

MEMBERS of the Alumni Fund Committee of the College of Medicine of New York University met at

a dinner on October 7 in New York City to plan the collection of a fund of $50,000 in preparation for the centennial celebration next year. Dr. Luther B. McKenzie is president of the Medical Alumni Association.

Speakers at the dinner included Dr. Harry Woodburn Chase, chancellor of the university; Dr. Samuel A. Brown, dean emeritus of the College of Medicine; Laurence G. Payson, chairman of the finance committee of the council of the university, and Dr. McKenzie. Dr. Currier McEwen, dean of the college, was toastmaster.

The College of Medicine of New York University opened in October, 1841. It has graduated 10,900 physicians. Approximately 5,000 alumni are now living. One out of each five physicians registered in New York City is an alumnus of the college.

The faculty has grown from a group of eight teachers in the first year to 507 on the instruction and clinical staff for the current academic year. The 1940–41 enrolment is 497 students, nearly ten times the 1841 enrolment of fifty-one students.

From its inception the college has been closely identified with Bellevue Hospital and has recently become affiliated with New York City in the development of a public health program. In addition it has conducted its own clinic for fifty-seven years and last year treated its one millionth patient.

The campaign for the alumni fund of $50,000, which will be used for the purchase of instructional equipment and for the support of the library and other special departments of the college, will be conducted by Dr. McKenzie and a committee of seventy graduates.

THE AMERICAN SOCIETY OF MECHANICAL ENGINEERS

As a result of a letter ballot of the 15,000 members of the American Society of Mechanical Engineers the following officers have been elected: William A. Hanley, director of Eli Lilly and Company, Indianapolis, Ind., and head of its engineering division, *president; vice-presidents* to serve two-year terms on the council: Samuel B. Earle, research engineer and dean of engineering at Clemson Agricultural and Mechanical College, South Carolina; Frank H. Prouty, a partner in the Prouty Brothers Engineering Company and the Industrial Appraisal Company, both of Denver, and Edwin B. Ricketts, mechanical engineer with the Consolidated Edison Company of New York, Inc., New York, N. Y.; managers elected to serve on the council for three-year terms: Huber O. Croft, professor of mechanical engineering and head of the department at the University of Iowa; Paul B. Eaton, consulting engineer and head of the mechanical engineering department at Lafayette College, and George E. Hulse, chief engineer, The Safety Car Heating and Lighting Company, New Haven, Conn.

The new officers will be installed during the sixty-first annual meeting, which will be held at the Hotel Astor, New York City, from December 2 to 6. Headquarters will be at the Hotel Astor instead of at the Engineering Societies Building. The meeting is expected to attract to it about 5,000 engineers and executives from the United States and Canada. More than a hundred technical papers on such specialized mechanical engineering subjects as aeronautics, applied mechanics, fuels, hydraulics, metals engineering, machine-shop practice, management, materials handling, petroleum, steam power, railroads, textiles, heat transfer and process industries, will be presented by leading experts in the field. To accommodate all these papers, forty-four sessions are being arranged, including six on Monday evening, December 2.

At the banquet on Wednesday evening, December 4, two addresses, one by the president of the society, Warren H. McBryde, of San Francisco, and the second by a member of the National Defense Commission, will be made. In addition, President McBryde will present the 1940 awards of the society, including the American Society of Mechanical Engineers Medal, the Holley Medal, the Worcester Reed Warner Medal, the Melville Medal, the Junior Award, the Pi Tau Sigma Award, the Charles T. Main Award of $150, and two Student Awards of $25 each. Tuesday evening will be devoted to an informal, get-together smoker, and Thursday evening to college-reunion dinners.

In addition to the technical sessions programs on "Training to Meet the National Emergency" have been arranged at 9:30 A.M. and at 2 P.M. on Thursday, December 5. The speakers and their subjects will include:

"Training for National Defense," by Dean A. A. Potter, Purdue University.

"Training in Industry to Meet the National Defense Program," by C. R. Dooley, manager of industrial relations, the Socony-Vacuum Oil Company, New York.

"Training College Graduates for the Aeronautic Industry," by H. Randall Irwin, the Lockheed Corporation, California.

"Important Training Being Done at the U. S. Navy Yard," by Captain Lake or Captain Fisher.

"Emergency Training Program Being Carried out at the Rensselaer Polytechnic Institute," by President William O. Hotchkiss and Professor Stanley Wiltse, of the institute.

"Need for Training on College and Sub-College Levels as Seen by the U. S. Civil Service Commission," by E. J. Stocking, of the commission.

SCIENTIFIC NOTES AND NEWS

A BUST of Dr. Albert Einstein has been presented to the University of California at Berkeley. It was given to the university by Hugo D. and Arthur A. Newhouse and was cast in bronze by Frederick W. Schweigardt. It has been placed in the main catalogue room of the library. Dr. Einstein posed for the bust in 1933 when he lectured at the California Institute of Technology in Pasadena.

REAR ADMIRAL RICHARD E. BYRD received from President Roosevelt on September 27 a gold star in recognition of the success of his Antarctic expedition.

DR. WILLARD COLE RAPPLEYE has received leave of absence for fifteen months from the deanship of the College of Physicians and Surgeons, Columbia University, to enable him to succeed Dr. Sigismund S. Goldwater as commissioner of hospitals. The oath of office was administered to Dr. Rappleye by Mayor La Guardia on October 1 in the World's Fair City Hall. Dr. Goldwater resigned recently as commissioner of hospitals to devote full time to his position as head of the Associated Hospital Service.

THE William Lawrence Saunders gold medal for 1941 of the American Institute of Mining and Metallurgical Engineers has been awarded to Herman C. Bellinger, vice-president of operations of the Chile Exploration Company, a subsidiary of the Anaconda Copper Mining Company. Mr. Bellinger, who will receive the medal in February at the annual meeting of the institute, was responsible for electrification of the Chuquicamata Mine in Chile and for the introduction of liquid-oxygen explosives for blasting at the mine. Robert Crooks Stanley, chairman of the board and president of the International Nickel Company of Canada, Ltd., will receive at the same meeting the first Charles F. Rand gold medal "for achievement in mining administration."

AT the recent fiftieth anniversary meeting of the New York State Library Association the guest of honor was Dr. Andrew Keogh, who was until recently librarian of Yale University.

CHARLES W. PATTERSON, registrar of Northwestern University Medical School for twenty-seven years, has been retired with the title associate professor emeritus of pharmacology. He had been associated with the school for forty-seven years.

DR. CHARLES T. CHAMBERLAIN, for many years clinical professor of otolaryngology at the Medical School of the University of Oregon in Portland, has retired with the title emeritus professor of otolaryngology.

DR. M. J. DORSEY, chief of the division of pomology at the College of Agriculture of the University of Illinois, has been appointed head of the department of horticulture. Dr. Dorsey succeeds Dean J. C. Blair, director emeritus, who organized the department and served as its first and only head for forty-three years.

DR. ROBERT D. LEWIS, a member of the department of agronomy of the Ohio State University, formerly professor of plant breeding at Cornell University, has been appointed head of the department of agronomy at the Ohio State University.

DR. JOHN W. CHAMBERLAIN, assistant in the department of hygiene at the Massachusetts Institute of Technology, has been appointed assistant director.

DR. PAUL A. NEAL, surgeon, U. S. Public Health Service, a member of the staff of the National Institute of Health at Bethesda, Md., has been detailed as chief of the division of industrial hygiene of the institute. He succeeds Dr. Royd Ray Sayers, who joined the staff of the U. S. Bureau of Mines several months ago.

DR. WILLIAM C. SENNING, of Cornell University, has been appointed head of a new research station established by the New York State Conservation Department at the University of Rochester, to improve production and management of fish in the Finger Lakes region and westward.

DR. GEORGE B. DARLING, associate director, and Dr. Emory W. Morris, associate executive director, of the W. K. Kellogg Foundation at Battle Creek, Mich., have been elected, respectively, president and general director, succeeding the late Dr. Stuart Pritchard, who held both positions.

DR. HELLMUT DE TERRA, research associate of the Carnegie Institution of Washington, has been appointed associate professor of geography at the New School for Social Research, New York, by special grant from the Rockefeller Foundation.

DR. ROBERT A. JEHLE, specialist in plant pathology for the University of Maryland Extension Service, has been appointed professor of plant pathology at the university and state plant pathologist. He succeeds Professor Charles E. Temple, who retired on October 1.

DR. OTTO HAAS, of Vienna, is cooperating as a volunteer worker in a research project based upon the collections of invertebrate fossils with members of the staff of the departments of geology and zoology at the Field Museum, Chicago.

F. C. BAWDEN, in charge of investigations on virus diseases of plants, has been appointed head of the

department of plant pathology at the Rothamsted Experimental Station at Harpenden, in succession to Dr. J. Henderson Smith, who is retiring after having held the post since 1932.

C. VERNON HOLMBERG, assistant in research sponsored by the Technical Association of the Pulp and Paper Industry at the New York State College of Forestry, spent the summer in research on wood waste utilization at the Miner Laboratories, Chicago.

A GRANT of $2,760 has been appropriated by the National Foundation for Infantile Paralysis (the President's Birthday Fund) for research by Dr. John A. Toomey, associate professor of pediatrics (contagious diseases) of the School of Medicine of Western Reserve University. It is to be used to find a method of producing infantile paralysis in the smaller animals. Dr. Toomey has previously received grants from the National Foundation amounting to $48,000 for his experiments in infantile paralysis at the City Hospital.

BY an Order of the Committee of the British Privy Council the Rt. Hon. James Gray Stuart has been appointed a member of the Medical Research Council in the vacancy caused by the resignation of R. K. Law, M.P. By another Order, made after consultation with the Medical Research Council and with the president of the Royal Society, Sir W. Wilson Jameson, dean of the London School of Hygiene and Tropical Medicine, has been appointed a member of the council in succession to Professor Matthew J. Stewart, professor of pathology at the University of Leeds, who retired in rotation on September 30.

SIR ARTHUR HURST gave the eighteenth Norman Kerr Memorial Lecture before the Society for the Study of Inebriety, London, on October 8. His subject was "Alcohol and the Organs of Digestion."

THE two hundred and thirty-seventh regular meeting of the American Physical Society will be held at the University of Chicago on Friday and Saturday, November 22 and 23. Other meetings for the current season are as follows: Pacific Coast meeting, Pasadena, Calif., December 20 and 21; annual meeting, Philadelphia, December 26 to 28; Cambridge, February 21 and 22; Washington, D. C., May 1 to 3, 1941; Providence, June 20 and 21, 1941.

THE Michigan-Indiana-Ohio Museums Association will hold its thirteenth annual meeting at Toledo, Ohio, on October 17, 18 and 19. The Toledo Museum of Art and the Toledo Zoological Gardens will be hosts for the meeting.

THE first meeting of the 1940–41 season of the Mid-West Section of the American Association of Cereal Chemists was held on October 7, with dinner at Somerset Poultry Farm Restaurant, Lyons, Ill. A short business session was held, after which J. M. Mercer, junior department engineer, Sanitary District of Chicago, spoke. The speaker took as his subject "A Half Century of Water Supply Practice for Chicago." An inspection trip through the main sewage disposal plant followed. Announcement is made that at the Tri-Sectional meeting at Urbana on November 9 the Mid-West Section will supply two speakers. Immediate past president of the national organization, George Garnatz, of the Kroger Grocery and Baking Company, Cincinnati, Ohio, will be the guest of honor.

THE fifth annual meeting of the Carolina Geological Society will be held at Bond Hall, The Citadel, Charleston, South Carolina, on October 19 and 20. Under the leadership of Professor J. H. Watkins the following places will be visited: on October 19 the Charleston Museum; Earthquake Evidence; Old Dorchester Road; Dump Shaft No. 11; Edisto-Goose Creek Tunnel; Summerville; Givhans State Park; Bee's Ferrybridge. There will be dinner at the Citadel Mess Hall at 7:30 P.M., which will be followed by a business meeting in the Physics Lecture Room. General Summerall will address the society at dinner. On Sunday there will be trips to the Santee-Cooper Project and to Eutaw Springs.

MEMBERS of the American Society of Naturalists are asked to submit nominations for new members to the secretary before the close of the forthcoming annual meeting. According to the constitution, nominations must be received before this time in order to be eligible for election in December, 1941. The secretary is Dr. Ralph E. Cleland, department of botany, Indiana University, Bloomington, Ind.

DR. ROY CHAPMAN ANDREWS, director, has announced that visitors admitted to or remaining in the American Museum of Natural History, New York, after 5 P.M. will be required to identify themselves. Identification may be established by showing to museum guards membership, registration or other cards indicating affiliation with the particular activity or agency using the museum premises. Those admitted to or remaining in the museum after 5 P.M. are expected to confine themselves to that part of the building designated for the activity for which they are admitted. It is understood that the rule will be applied gradually and discreetly, so that no person with legitimate business after hours will be embarrassed or inconvenienced. This request of the museum in no way indicates that friends of members may not attend meetings also, but should they do so, it is hoped that they will be prepared to prove their contact with a particular member and occasion. Members of the New York Academy of Sciences are, therefore, requested to

carry their current membership cards when attending meetings, and to be prepared to show them to museum attendants if requested to do so.

REPORTS received by the editors of *Chronica Botanica* stated that the collection of cultures of the Central Bureau of Fungus Cultures in Baarn, Holland, is in excellent condition and has not been damaged by the war. Shortly before the invasion of the Netherlands tentative plans had been made to transfer part of this collection to the United States, as it contains many types of great importance to American mycologists and phytopathologists.

ACCORDING to the *Journal* of the American Medical Association, the medical department of the University of Chicago eventually will receive all of the estimated $100,000 estate of the late William O. Oppenheim. Under a trust established by the will, the income will go to relatives during their lifetime.

IT is reported that the construction of a new library in the Harvard yard, to house rare books and manuscripts and to provide exhibition and study rooms for important collections, will be begun this autumn. The new building, 55 by 120 feet, will be situated east of Widener Library. It will be of Georgian style, brick and limestone, three stories above ground, housing more than a quarter of a million volumes. The structure has been made possible through the support of an anonymous alumnus. One of the most important collections of sixteenth and seventeenth century material in the United States, now in Widener Library, and all the books in the Treasure Room will be moved there. This transfer will relieve in part the critical shortage of space in the library.

NOMINATIONS are solicited for the 1941 award of $1,000 established by Mead Johnson and Company to promote researches dealing with the B-complex vitamins. The recipient will be chosen by a Committee of Judges of the American Institute of Nutrition and the formal presentation will be made at the annual meeting of the institute at Chicago on April 16, 1941. The award will be given to the laboratory or research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year the most meritorious scientific report dealing with the field of the B-complex vitamins. Membership in the American Institute of Nutrition is not a requisite of eligibility for the award. Nominations for work published in 1940 must be in the hands of the secretary by January 25, 1941. They should be accompanied by such data relative to the nominee and his research as will facilitate the task of the committee in its consideration of the nominations. Correspondence should be addressed to Dr. L. A. Maynard, secretary of the American Institute of Nutrition, Laboratory of Animal Nutrition, Cornell University, Ithaca, New York.

THE *Journql* of the American Medical Association states that the Chicago Heart Association, Inc., has received from the Clara A. Abbott Trust a gift of $27,000 to be added to the Memorial Fund founded in memory of Morris Fishbein, Jr. The money is to be used either by itself or with other funds of the society for the study and treatment of diseases of the heart and the circulation. A fellowship is to be established in a hospital or medical school in Chicago, which will be devoted primarily to the study of the cause and treatment of rheumatic fever. The Clara A. Abbott Trust has already donated millions of dollars to the University of Chicago, to Northwestern University and to the Evanston Hospital, since the purpose of the Clara A. Abbott Trust is to aid the care of the sick and the advancement of medical science. The Memorial Fund of the Chicago Heart Association, now almost $40,000, was established in 1929 by Dr. Morris Fishbein, editor of the *Journal* of the American Medical Association, and Mrs. Fishbein, at the time of the death of their son from rheumatic fever. The fund is administered by a self-perpetuating committee of five, including Drs. Robert B. Preble, Newell C. Gilbert, James B. Herrick, Walter W. Hamburger and Morris Fishbein.

THE *Lancet* reports that the outbreak of war had an unfortunate paralyzing effect on organized medical research, more particularly on the work of the special institutes in London whose staffs were dispersed to the various sectors or to emergency public-health laboratories throughout the country. The Lister Institute, with the exception of its biochemical and biophysical departments, shared in the general exodus, but it had at Elstree a country home for its bacteriological staff, the division of nutrition was accommodated at Cambridge, while individual members of the staff found refuge in other research institutes. As a result, the latest annual report, giving an account of the extensive researches in bacteriology, nutrition and biochemistry of the institute, bears little imprint of disorganization.

DISCUSSION

EDUCATION AND PARTICIPATION IN SCIENCE

LAYMEN scientists or amateurs from time to time have made important contributions to research in the physical and natural sciences. Such persons, although lacking professional training, often become experts in their field and learn the spirit and method of science through actual apprenticeship. To test the effective-

ness of such work on the part of amateurs, as well as to bridge the gap between the general public and pure research, has been the purpose of a program in the Philadelphia area conducted by the Committee on Education and Participation in Science under the supervision of The American Philosophical Society since June, 1939. The grant from the Carnegie Corporation of New York, which has made this work possible, was renewed to extend until June, 1941. The members of the society who comprise the committee are: Dr. E. G. Conklin, *chairman;* Dr. Anton J. Carlson, Dr. Karl K. Darrow, Dr. Luther P. Eisenhart, Dr. C. E. Kenneth Mees, Dr. Oscar Riddle, Dr. Harlow Shapley, Dr. George G. Simpson, Dr. W. F. G. Swann, Dr. Edward L. Thorndike, Dr. Harold C. Urey and Mr. Roland S. Morris, president of the American Philosophical Society. For the past fourteen months, the committee has made an intensive survey of the amateur scientific movement through both questionnaires addressed to individuals and a study of amateur clubs and societies. The results of this work are now being prepared for publication in the form of a pamphlet entitled, "The Layman Scientist in Philadelphia: A Directory of Amateur Scientific Organizations and Resources in Science."

More recently, beginning April 1, 1940, a series of programs has been carried out by the committee whereby amateur scientists in the Philadelphia area, working on a voluntary basis, are making original observations and compiling data in the fields of botany, climatology, physics and radio, and zoology under the supervision of professional scientists. These consultants are attached to the committee's executive staff. In botany, eighty laymen observers in suburban localities near Philadelphia have been engaged in a phytophenological study. In the course of this work they have recorded, in systematic form, the opening of petals, the shedding of pollen and the maturing of fruit of some 115 of local spring and summer wild flowers. The records included weather observations and other notes which were made on mimeographed charts supplied by the committee. The study was planned and directed by Dr. John M. Fogg, Jr., assistant professor of botany of the University of Pennsylvania and consultant to the committee. At the same time, another group of men and women, under the supervision of Dr. Edward E. Wildman, of the Philadelphia Board of Education and also a staff member, are participating in a study of tree ring growth in relation to the climate of the Delaware Valley included in eastern Pennsylvania, southern New Jersey and parts of Delaware and Maryland. Over one hundred individuals have already supplied data on the location of stumps and cross-sections of trees one hundred years or more in age. Some of the participants have made paper strip records indicating the relative thickness of the growth rings, not only in tree stumps but of the cross-sections from timbers of ancient dwellings. It is planned that the information will be collected and used in the compilation of master charts which will be available for study by professional dendrochronologists. The committee issues, from time to time, a mimeographed "Tree Ring Log" which contains letters and notes from the amateurs engaged in this project as well as information concerning old diaries, letters and newspaper accounts which reveal the past weather history of the Philadelphia region and which are being uncovered by volunteer students.

Radio communication and a phase of its relation to physics concerns the third project for laymen volunteers. This program, under the direction of Dr. Serge A. Korff, of the Bartol Research Foundation and consultant in physics and astronomy to the committee, involves a study of the ionosphere or Heaviside layer. Amateur radio operators who agree to cooperate filll out charts with technical information concerning receptions, fade-outs, skip-distance records and other data obtained in the course of their normal contacts. More than two hundred persons have commenced active participation in this study and have sent in several hundred important records. One member of the group contributed many hours of his time in compiling the data already accumulated, which will eventually be used in the ionosphere investigations carried on by Dr. L. V. Berkner, of the Carnegie Institution of Washington.

A fourth experiment for the Philadelphia amateurs has been undertaken in the field of zoology under the leadership of Mr. Roger Conant, of the committee's executive staff, who is also curator of the Philadelphia Zoological Garden. During the past summer some thirty amateur naturalists have made intensive local studies of reptiles, amphibians and insects by tagging or otherwise marking them and studying their feeding, growth, mating and other habits. In some cases these studies have involved the devising of original techniques on the part of the volunteers. Frogs and turtles have been the animals most frequently employed.

In all these programs the work has been entirely voluntary. Close touch is kept with the various persons who cooperate and informal meetings and discussions are held by the scientists of the committee's executive staff who supervise the projects. The volunteers represent dwellers in urban and suburban communities with varied occupations and interests, including business men, stenographers, engineers, housewives, teachers and others. The amount of time devoted to this work attests to the enthusiasm which has been aroused. Many of the persons taking part have expressed their satisfaction in being permitted to do experimental work in some field of science, even if the duties often

comprise the laborious one of making detailed observations and recording data. Since June, 1940, four radio talks have been presented by the consultants of the executive staff. These talks on various phases of the committee's programs for amateurs included two nation-wide broadcasts in cooperation with the series of "Adventures in Science" of Science Service on the Columbia Broadcasting System. One result of these talks and other forms of publicity has been an increasing interest in amateur scientific programs for other sections of the country. Starting in October the committee will resume the monthly publication of its circular, "Activities in Science in the Philadelphia Area," which lists a variety of educational opportunities in the physical and natural sciences, such as lectures, demonstrations, field trips, exhibits and radio broadcasts. It also includes notices of the regular meetings of the forty amateur scientific societies in the region. An interesting development of the activities of the committee has been the formation of the Philadelphia Council of Amateur Scientists which will hold its first formal meeting on September 23. Delegates from all the active groups will be present.

Further information concerning the American Philosophical Society's Committee on Education and Participation in Science can be obtained from W. Stephen Thomas, Executive Secretary of the Committee, The American Philosophical Society, 104 South 5th Street, Philadelphia, Pennsylvania.

W. STEPHEN THOMAS

VEGETATION TYPE MAPS OF CALIFORNIA AND WESTERN NEVADA

IN order to obtain information needed in a variety of administrative and research problems, the Forest Survey Division of the California Forest and Range Experiment Station[1] has for some years been mapping the natural vegetation resources of California and western Nevada. Twenty-one of the map units have been published to date.[2] Each unit consists of a standard 15- or 30-minute U. S. Geological Survey topographic quadrangle (approximately 1- or ½-inch to the mile, respectively) on which symbol and color overprints have been placed to show, as far as the base permits, the present dominant vegetation just as it occurs on the ground. On wide margins are the legend; brief descriptions of the type classification basis and the various types found on the quadrangle; a table summarizing the type areas by counties, national forests and parks; and a profile illustrating the relationship of types to elevation and slope exposure.

Plant associations, based upon dominant species composition, comprise the primary vegetational elements mapped. These are shown in their actual relation to the topography, with symbols identifying the species involved. Any species is considered a dominant if it forms 20 per cent. or more of the total vegetation cover in associations that are wholly herbaceous, shrubby or arborescent; or like percentages of its respective class in composite associations. These percentages are applied only to the vegetation visible from above, however, since the mapping is done externally. The associations are segregated according to general similarities of use, economic importance and fire-hazard characteristics into broad types, which are designated by colors. Three of these types are classed as herbaceous, 5 as shrubby, 4 as broadleaved tree, and 10 as coniferous tree. Also shown are barren, semi-barren and desert areas, cultivated and urban lands and tree plantations.

A considerable amount of basic information concerning the present vegetation resource is thus made available for ready use. The color designations alone are ample for many purposes in which only broad classes of vegetation are involved. If it should be necessary to modify the grouping or to obtain certain details of species composition, the individual associations and their included symbols may be used. In either case the distributions may be studied in relation to location and area occupied, elevation and slope exposure. Although successional positions are not directly indicated, a knowledge of the ecological relationships of the local flora will provide the clues for such a classification.

This flexibility opens up a wide range in usefulness. In California, the maps have had important parts in many projects dealing with the protection, management and utilization of the resource they depict, and in botanical, zoological, ecological and geographical studies as well. For classroom study and demonstration their use has been wide-spread. As the significances of the different elements making up the resource become better understood, these and other uses will grow. Whatever may be lost through lack of agreement with actual conditions after vegetational changes have occurred will be more than compensated by the increasing value of a record against which conditions of the future may be compared.

Other maps of this series will be published as rapidly as funds become available for that purpose.

H. A. JENSEN

CALIFORNIA FOREST AND RANGE EXPERIMENT STATION

[1] Maintained by the U. S. Department of Agriculture at Berkeley, Calif., in cooperation with the University of California.

[2] Obtainable at the cost of printing from the University of California Press, Berkeley, Calif.

SEX VARIATION IN THE UTILIZATION OF IRON BY ANEMIC RATS

IN the issue of SCIENCE for June 28, 1940, Dr. Mary Swartz Rose calls attention to our article entitled

"Further Evidence of Sex Variations in Utilization of Iron by Anemic Rats," and states that the findings of the authors, Drs. Louise Otis and Margaret Cammack Smith, "were previously established by Dr. Helen Hubbell and reported in the *Journal of Nutrition* in January, 1938, Vol. 15, pp. 91–102." In this connection we would like to point out that in the course of an investigation using hundreds of rats, begun in 1935 in our Arizona laboratories on the hematopoietic value of foodstuffs, a marked difference in the response of male and female rats was consistently noted. At that time it was current practice in other laboratories to use male and female rats interchangeably, which gave conflicting results. Our findings were reported in a paper by Smith and Otis entitled "Sex Variations in the Utilization of Iron by Anemic Rats," which appeared in SCIENCE in January, 1937, Vol. 85, pp. 125–6, which was almost a year before the paper by Rose and Hubbell appeared. Also, a paper by Smith and Otis entitled "Hemoglobin Regeneration in Anemic Rats in Relation to Iron Intake," which included a discussion of their findings concerning sex difference, was published in the *Journal of Nutrition,* Vol. 13, pp. 557–82, in June, 1937.

We regret that in our third paper, entitled *"Further Evidence* of Sex Variation in Utilization of Iron by Anemic Rats," which is the paper to which Dr. Rose refers, no mention was made of the excellent paper of Rose and Hubbell. It would, of course, have been included in any complete review of the literature on the subject, but a review of any length is not permitted in SCIENCE. A more complete description of our iron studies is soon to appear elsewhere.

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SUGGESTIONS REGARDING A PROPOSED STANDARDIZATION OF OSMOTIC PRESSURE AS A TERM

THE proposal to standardize osmotic pressure as a term made recently in these columns[1] should meet with sincere approval. We believe, however, that such a standardization should, if possible, transcend the limits of one field of science. This is particularly necessary from a pedagogical standpoint.

As pertinent to this suggestion we would call attention to the desirability of considering osmotic pressure as the pressure that must be exerted on the solution in order to make the escaping tendency of the solvent from the solution equal to the escaping tendency of the pure solvent at the same temperature. One needs further to point out that (*a*) the addition of a solute to a solvent in general lowers the escaping tendency of the solvent molecules and (*b*) the application of an external pressure in general increases the escaping tendency of the solvent. This treatment of osmotic pressure is quite generally found in the better elementary text-books of chemistry, in the physical chemistry texts and in advanced texts.[2]

It will be observed that the suggested standardization includes the two generalizations regarding the influence of solute concentration and pressure. We propose (1) that the definite relation between these generalizations and the osmotic pressure be pointed out and (2) that reference be made to some generalized term such as "escaping tendency."

We suggest that such an amplification would improve the treatment of the term by increasing the range of applicability and by relating the phenomenon under consideration to others, such as vapor pressure effects, etc.

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SCIENTIFIC BOOKS

LIFE ON OTHER WORLDS

Life on Other Worlds. By H. SPENCER JONES. New York: The Macmillan Company. 1940.

FOR centuries man has wondered and speculated about the possibility of life on other worlds. Nowadays probably no question is put more frequently to the astronomer by the layman than "Are there men on Mars?" Percival Lowell at the close of the past century thought he had evidence for the existence of intelligent life on Mars. Alas, the modern astronomer can not concede Lowell's point. H. Spencer Jones, Astronomer Royal of England, in his recent book, "Life on Other Worlds," brings a timely and authoritative account of many aspects of the problem of the existence of life elsewhere in the universe.

Regardless of whether or not life does exist on the other planets, life can be directly observed only on the Earth. Life as we know it must therefore furnish a working definition of what shall constitute life. Complex molecules containing carbon have been found to form the basis of the structure of all living organisms on Earth. From the prevalence of the same physical

[1] H. C. Eyster, SCIENCE, 92: 171–2, 1940.

[2] The following list includes an example from each of the classes mentioned: Herman T. Briscoe: "An Introduction to College Chemistry," p. 257. Houghton Mifflin Company. W. H. Rodebush and E. K. Rodebush: "An Introductory Course in Physical Chemistry," p. 188. D. Van Nostrand Company. G. N. Lewis and Merle Randall: "Thermodynamics and the Free Energy of Chemical Substances," p. 213. McGraw-Hill Book Company.

and chemical laws throughout the universe, Dr. Spencer Jones consequently infers that the formation of similar large molecules with chainlike structure and of feebly stable molecular groups must be possible wherever living matter is to exist, although the living matter need not necessarily be of a type familiar on Earth. A study of the physical, meteorological and geological conditions and their evolution on the Earth make it evident that the requisites for the existence of life (especially regarding atmospheric composition and temperature) are rather narrowly defined. Spencer Jones, discussing at length all the planets and the principal satellites of the solar system, finds evidence for vegetation on Mars, but no evidence anywhere for animal life. With the possible exception of Mars, the Earth is, he contends, the only planet on which animal life can have developed.

Speculatively the author also takes us beyond the solar system. Considering the nicety of conditions required for the existence of life, may we egotistically assume that we are the only men in the universe, or must we modestly admit that our Earth is but one among innumerable similar satellites to other suns? That, according to the Astronomer Royal, depends very much on how the solar system originated. Many theories have been proposed, but all, on careful examination, have been found wanting. The most promising theory requires such specialized accidental circumstances that our egotism is encouraged. On the other hand, he points out, the immensity of the number of galaxies of stars and the theory of an expanding universe combine to suggest that ours is not a unique world.

"Life on Other Worlds" gives a fairly complete survey of the present state of knowledge on the subject. It is fluently and clearly written. In general, the treatise is not only instructive but entertaining (notably where the fates of would-be rocket exploring-expeditions to the Moon are commented upon) and it is definitely provocative of thought. The reader is left impressed with the quantity of research in numerous fields of science that has been accomplished in an approach to the solution of the problem of life elsewhere in the universe. "Life on Other Worlds" is sincerely recommended to all astronomically and philosophically minded laymen. For the astronomer it will provide an enjoyable "busman's holiday."

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MEDICINE IN AVIATION

Grundriss der Luftfahrtmedizin. By SIEGFRIED RUFF and HUBERTUS STRUGHOLD. viii + 191 pp., 103 figs. Leipzig: Johann Ambrosius Barth, Verlag. 1939.

THE preface to this book is written by Dr. E. Hippke, "Chef des Sanitätswesens der deutschen Luftfahrt." Chapter I reviews the problems which meet the aviator and alpinist as higher and higher altitudes are reached. Chapter II contains an analysis of different factors affecting the organism in high altitude: the low pressure of oxygen, the low temperature, the ultra-violet radiation, etc. A short review of the general physiological and physical background necessary for understanding the special physiology of high altitude is given in the first part of the chapter; later follow descriptions of the effects on organs and functions and of ways for investigating and combating the impairing forces. Problems of practical importance, as acclimatization to high altitude, high altitude tolerance, oxygen administration, etc., are given special consideration. Chapter III deals with acceleration. In this field, new as it is, the Germans are specialists in research and in the application of research. Centrifugal force has been studied both "artificially" by means of great centrifuges and "naturally" in various kinds of diving, "pull-outs," "looping," etc. Air-sickness is considered in this chapter. Chapter IV covers the psychophysiology of aviation, especially sensory physiology. In Chapter V the reasons for accidents in flying are analyzed and devices apt to diminish them described, and in Chapter VI is given a short but inclusive review of the comparative physiology of flying.

The book is offered as a supplementary text for students of medicine and as a source of orientation and information for practical men—aviators, military men, physicians and people interested in the problems of the man in the air force. Most figures, tables, curves, etc., are taken from German sources. An English translation might properly include a supplementary chapter or appendix containing data from American and other sources. A revision of the bibliography along the same lines also would seem advisable.

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CHEMISTRY IN WARFARE

Chemistry in Warfare. By F. A. and M. S. HESSEL and WELLFORD MARTIN. With a foreword by Colonel Crosby Field and a Technical Appendix. New York: Hastings House, 135 Front St. 164 pages; numerous illustrations and diagrams; price, $2.00. 1940.

THIS popular treatment of the subject is clearly and interestingly written. Its purpose is to give the layman a concise and reasonably comprehensive review of the manifold ways in which modern warfare is dependent upon chemistry and the chemist, with such illustrations, diagrams and collateral information as will enable any one to see for himself the significance of chemistry's rôle and the indispensability

of the chemist in any program of preparedness and defense.

The subject-matter is assembled under the following chapter headings: I. The Soldier, II. Man-made Man-killers, III. Machines of Modern Warfare, IV. Crucibles of Death (warfare with toxic chemcials), and V. The Chemical Industry—America's First Line of Defense.

The book is not written for chemical or military experts, and such may find minor flaws here and there but, in the opinion of the reviewer, it fulfils creditably its mission of presenting the subject to the uninitiate in a form which he can assimilate with ease and satisfaction and which will equip him to follow more intelligently the war news of the day. If he is a military man, it will teach him something about chemistry. If he is a chemist, he will gain some useful elementary knowledge of military equipment and tactics.

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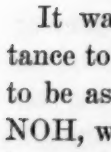
SPECIAL ARTICLES

A NEW CHEMICAL REACTION WITH THE NITROSYL RADICAL NOH[1]

MANY years ago I made the assumption that the nitrosyl radical, NOH, functions as the most important compound as far as the nitrogen in the synthesis of simple naturally occurring, carbon-nitrogen containing material is concerned.[2] It acts as a branching-point, leading to several series of compounds. The most important organic compounds synthesized by sunlight from KNO_2 and methyl alcohol or formaldehyde, which we have analyzed, are formhydroxamic acid,



, and formaldoxime, $CH_2=NOH$.

It was of special biochemical interest and importance to find other reactions involving nitrosyl. It was to be assumed that the strongly paramagnetic radical, NOH, would combine with inserted paramagnetic ethylene groupings which are present in the benzene ring and in many substituted benzene compounds.

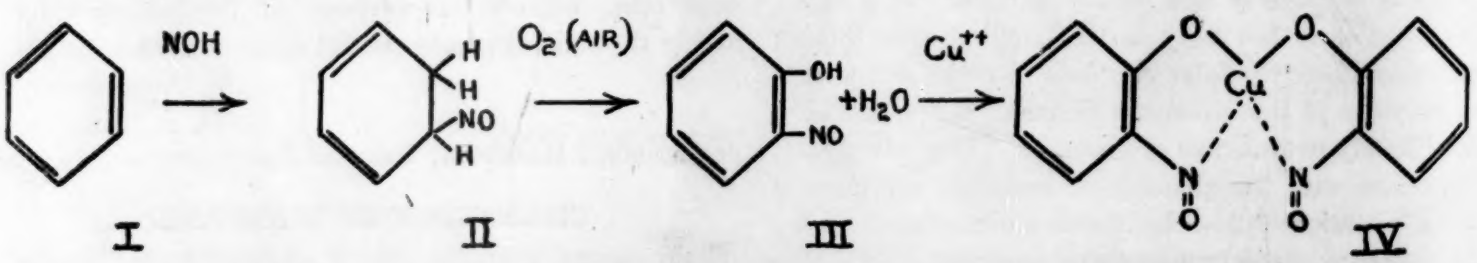
In this publication I will demonstrate that two groups, namely, NO and OH, can be substituted in benzene in a new, amazingly simple way at ordinary temperature. I will further try to elucidate the mechanism of the new chemical reaction with the radical NOH—a chemical process which will have a wide application in chemistry.

Exp. 1

0.5 g freshly prepared yellow cuprous hydroxide, CuOH, is suspended in 200 cc dist. water in which 0.5 g KNO_2 is dissolved (pH 9.9). Purest benzene is added and the solution well stirred. With dilute hydrochloric acid the pH is now adjusted to 2.5 and then 1 cc Merck's superoxol is added. The pale yellowish color changes immediately to pink and becomes deep red after longer stirring. The deep red *o*-nitrosophenol coppersalt (IV) forms *o*-nitrosophenol (III) on acidifying with HCl which can easily be extracted with petrol ether. The petrol ether solution is a beautiful green.

Exp. 2

0.5 g KNO_2 and 1 g cupric nitrate are dissolved in 200 cc dist. water (pH = 5.6). Purest benzene is now added



to the pale green solution and the whole mixture well stirred. On adding 1 cc Merck's superoxol the color remains green but becomes only a little darker. Now 0.5 g iso-ascorbic acid (or vitamin C) is added. The color immediately changes to pink and becomes deep red on further stirring (pH = 3.4), thus forming again *o*-nitrosophenol coppersalt (IV).

Exp. 3

0.5 g freshly prepared cuprous hydroxide is suspended in 200 cc dist. water in which 0.5 g benzene-sulfohydroxamic acid was dissolved (pH = 4.4). Purest benzene is added and the whole mixture well stirred. The pH is now adjusted to 2.9 by adding dilute hydrochloric acid. The solution quickly turns pink by autoxydation. By

In my recent experiments with hydroxylamine-hydrochloride, copper ions and benzene,[3] nitrosophenol copper salt (IV) was easily formed by autoxydation of the reaction mixture or still better by adding hydrogen peroxide. This remarkable reaction has since been successfully applied by us to many aromatic hydrocarbons and to a great number of substituted benzene compounds, of which more will be said in another journal.

[1] Part of the lecture presented at the A.A.A.S. symposium at Gibson Island, Maryland, July 22–26, 1940.

[2] Collected literature of the subject: Oskar Baudisch u. Lars A. Welo; *Chem. Rev.*, Vol. 15, no. 1, 1934.

[3] *Naturwissenschaften*, 27: 768–9, 1939; *Chem. Abstracts*, 34: 1976, 1940.

adding 1 cc Merck's superoxol a deep red color immediately appears. After one hour stirring, the red solution is acidified with dil. HCl and extracted with petrol ether. The now deep green petrol ether contains pure *o*-nitrosophenol. The aqueous layer remains deep red. It contains coppersalt of *o*-nitrosophenol sulfinic acid (see exp. 4).

Exp. 4 (without benzene)

0.5 g cuprous hydroxide is suspended in 200 cc dist. water in which 0.5 g benzene sulfo-hydroxamic acid was dissolved (pH = 4.4). The pH is now adjusted to 2.9. After putting 1 cc Merck's superoxol in the well-agitated solution, the brownish liquid turns deep red with a violet tint. After one hour, the liquid is acidified with HCl and shaken with petrol ether. Nothing goes into the petrol ether and it remains colorless. With ether, however, the *o*-nitrosophenol sulfinic acid can be extracted. The yellowish green ether solution gives characteristic colors with many metals, just like the free *o*-nitrosophenol. Deep red copper, green ferrous, greyish brown cobalt, red nickel and red mercury salts are formed.

From the four experiments described, one can notice that the radical, nitrosyl, has been formed in three different ways—(1) oxidation of $NH_2OH \cdot HCl$ with cupric ions, forming cuprous ions; (2) reduction of HNO_2 with cuprous ions; (3) NOH released from benzenesulfo-hydroxamic acid by adding copper ions plus H_2O_2.

In experiment 3, the NOH is partly captured by the benzene present in the reaction mixture and, therefore, *o*-nitrosophenol copper besides red *o*-nitrosophenol sulfinic acid copper is formed. On acidifying, the *o*-nitrosophenol goes easily into petrol ether while the free *o*-nitrosophenol sulfinic acid is only soluble in ether or ethylacetate.

In experiment 4, the NO and OH substitute hydrogen atoms in the benzene ring of the formed sulfinic acid (the exact position of the chelate NO–OH grouping will be later determined).

Without going into detail here as to the mechanism of the reaction, I assume that primarily both NOH and benzene (toluene, ethylbenzene, xylene, etc.) are coordinately linked to the cuprous ion and thus activated by rearrangement of the the electronic system. The whole reaction occurs, so to say, in the inner sphere of the Werner copper complex, which might be a cuprous or a cuprous-cupric complex. However, only the cuprous central atom of the complex seems to be able to link benzene coordinately. On oxidation to the cupric form it is again released. The reaction between the activated benzene and nitrosyl could be written schematically in the following way:

Compound II is autoxidizable and forms Compound III. The cuprous-cupric complex is stable only in a small range of pH (2.1–4), and in this pH range the best results are obtained. Addition of small amounts of acetone or acetonylacetone to the reaction mixture prevents the formation of *o*-nitrosophenol from benzene entirely. By using the new reaction, we have already synthesized about sixty new *o*-nitrosophenol compounds, all of which show the characteristic of the chelate grouping, ortho NO–OH, towards metals. At the same time many interesting properties are developed by the different substitutes in the benzene ring in different (*o.m.p.*) positions of which we will have more to say in another paper.

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THE FUNCTIONS OF DIPHOSPHOTHIAMINE (PHOSPHORYLATED VITAMIN B_1)

IN 1937, Lohmann and Schuster[1] identified *cocarboxylase* as diphosphothiamine. This important discovery, coupled with the work of Peters and his collaborators[2] on the necessity of vitamin B_1 for oxidation of pyruvate by the brain of avitaminotic pigeons, brought one more vitamin within the group of enzyme components. Soon after Lohmann's discovery, Lipmann[3] demonstrated that diphosphothiamine is one of the components of α-ketonoxidase, and Barron and Lyman[4] found that diphosphothiamine acted in animal tissues and bacteria as a catalyst not only for the decarboxylation and oxidation of pyruvate, but also for its dismutation.

The mechanism of this catalysis is still unexplained. It does not seem to be a reversible oxidation-reduction system, as riboflavine and nicotinic acid derivatives were shown to be, although such a theory was suggested by Lipmann.[5] In fact, a comparative study of the rates of reduction and reoxidation of thiamine and diphosphothiamine has shown that the vitamin becomes with phosphorylation more resistant to the action of reducing and oxidizing agents (Barron and Lyman[6]). Nor does it seem to act according to Langenbeck's theory,[7] for Stern and Melnick[8] have presented evidence against a "Langenbeck cycle" involving the amino groups in the pyrimidine ring. The multiple catalytic functions of diphosphothiamine suggest the possibility that it acts by forming the integral part of the activating protein of the enzyme systems concerned with the activation of pyruvate. Once the pyruvate is activated, it may react with catalysts for its oxidation, reduction, dismutation or condensation. This hypothesis need not postulate reversible oxida-

[1] K. Lohmann and P. Schuster, *Biochem. Zeits.*, 294: 188, 1937.
[2] R. A. Peters, *Chem. Weekblad*, 34: 26, 1937.
[3] F. Lipmann, *Nature*, 140: 25, 1937.
[4] E. S. G. Barron and C. M. Lyman, *Jour. Biol. Chem.*, 127: 143, 1939.
[5] F. Lipmann, *Nature*, 138: 1,097, 1936.
[6] E. S. G. Barron and C. M. Lyman. To be published.
[7] W. Langenbeck, *Ergeb. Enzymforsch.*, 2: 314, 1933.
[8] K. G. Stern and J. L. Melnick, *Jour. Biol. Chem.*, 131: 597, 1939.

tion-reduction; it predicts, on the other hand, more catalytic functions for the vitamin than those hitherto known.

To test the validity of this hypothesis, experiments were performed with white rats fed with a vitamin B_1 deficient diet. The degree of deficiency was followed by the loss of weight and by the determination of blood pyruvate. Rats fed with the same diet plus added vitamin B_1 were used as controls.

The mechanism of the synthesis of carbohydrates from pyruvate by liver slices, a synthesis discovered by Benoy and Elliott,[9] was first studied. If such a synthesis starts with the formation of phosphopyruvic acid from pyruvate and fumarate, aerobically:

$$\text{Pyruvate} + \text{fumarate} + H_3PO_4 + {}_3O_2 \rightarrow \text{Phosphopyruvate} + 4\ CO_2 + 2\ H_2O,$$

Phosphorylated vitamin may accelerate the synthesis of carbohydrate by activating the pyruvate in this primary reaction. Kidney slices of normal rats synthesized 9.93 mgs of carbohydrate per gram of fresh tissue in the presence of pyruvate (372 per cent. increase over the control) and 11.6 mgs in the presence of pyruvate plus fumarate (452 per cent. increase); the addition of vitamin B_1 did not increase these figures. Kidney slices of avitaminotic rats, on the other hand, synthesized only 5.35 mgs of carbohydrate with pyruvate (a 46 per cent. decrease compared to the control) and 5.15 mgs with pyruvate plus fumarate (55 per cent. decrease); on addition of vitamin B_1 there was a synthesis of 11.86 mgs of carbohydrate. In other words, vitamin B_1 restored to normal the rate of carbohydrate synthesis by the kidney slices of avitaminotic rats (Table I).

TABLE I

SYNTHESIS OF CARBOHYDRATE BY RAT KIDNEY SLICES*

Added substrate	Mgs glucose per gm fresh tissue	
	Normal	Avitaminotic
No substrate	2.10	2.54
Pyruvate (Pyr.)	9.93	5.35
Pyr. + fumarate	11.20	5.15
Pyr. + fum. + B_1	11.20	11.86

* Incubated for 3 hours at 38° in $NaHCO_3$-Ringer buffer with O_2: CO_2 as gas phase; pH, 7.4. The values given are average values of several experiments. Pyruvate, 0.08 m.M.; fumarate, 0.04 mM; vitamin B_1, 50γ or 50 micrograms.

The next reaction studied was the formation of citric acid by pyruvate and oxaloacetic acid, a reaction discovered by Knoop and Martius:[10]

$$\text{Pyruvate} + \text{Oxaloacetate} + \tfrac{1}{2}\ O_2 \rightarrow \text{citrate} + CO_2.$$

Phosphorylated vitamin B_1 may accelerate the synthesis of citric acid by activating the pyruvate which takes part in this reaction. Chopped heart of control rats produced 3.32 mgs of citric acid after 30 minutes' incubation with pyruvate and malate (malate goes readily into oxaloacetate) and 3.39 mgs on addition of vitamin B_1. When fumarate was used instead of malate, there was 20 per cent. less citric acid formed. The synthesis of citric acid by the heart of avitaminotic rats was decreased by 50 per cent. with pyruvate and malate and by 73 per cent. with pyruvate and fumarate as substrates. The lack of increase in the synthesis of citric acid on addition of vitamin B_1 must be attributed to lack of its phosphorylation during the short time of its incubation. In fact, when rat kidney slices of avitaminotic rats were incubated with vitamin B_1 previous to the addition of substrates, there was an increase of 35 per cent. (Table II).

TABLE II

SYNTHESIS OF CITRIC ACID BY CHOPPED HEART AND KIDNEY SLICES OF RATS*

Added substrate	Mgs citric acid per gm fresh tissue	
	Normal	Avitaminotic
Heart—No substrate	None	None
Pyr. + malate	3.32	1.61
Pyr. + malate + B_1 ...	3.39	1.65
Pyr. + fumarate	2.64	0.75
Pyr. + fumarate + B_1 .	2.76	0.67
Kidney—No substrate		None
Pyr. + malate		0.60
Pyr. + malate + B_1 ...		0.81

* Incubated for 30 minutes at 38° in phosphate-Ringer; pH, 7.4; O_2 as gas phase; pyruvate, 0.134 m.M; l-malate and fumarate 0.186 mM. Total volumes 3 cc.

These *in vitro* experiments show that the synthesis of carbohydrates and of citric acid with pyruvate as one of the substrates is diminished in tissues from avitaminotic rats, and is increased on addition of vitamin B_1. They are offered as evidence for our view that vitamin B_1 is a catalyst not only for the oxidation and decarboxylation of pyruvate but also for many other reactions where pyruvate is one of the reacting substances.

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BIOELECTRIC POTENTIAL AS INDICATOR OF OVULATION IN THE HEN

IN order to discover bioelectric potential differences connected with the physiology of normal reproduction in the mature fowl a D. C. millivoltmeter[1] was applied to laying hens. The possibility of recovering the egg easily, as well as the fact that the fowl has only one functional ovary, made this species particularly suitable for the experiment.

While the experiments are still under way, some preliminary findings can be reported here.

[9] M. P. Benoy and K. A. C. Elliott, *Biochem. Jour.*, 31: 1,268, 1937.

[10] F. Knoop and C. Martius, *Zeits. physiol. chem.*, 242: 1, 1936.

[1] Modification by Dr. R. Parmenter of Burr, Nims, Lane apparatus.

Using silver silver-chloride electrodes in saline solution as a medium of contact, two laying hens were tested in their potential difference between the two sides of the abdomen. Table I gives the results of the test.

TABLE I

BIOELECTRIC POTENTIAL DIFFERENCE IN 2 LAYING HENS AT DIFFERENT STAGES OF REPRODUCTION

Hen	Date	Hour	Last egg	MV	Next egg
S	June 6	1:15 P.M.	1:00 P.M.	− 3.8	
		1:25 "		−26.6	June 7 noon
		1:35 "		−19.0	
	June 7	2:00 "	12 noon	−11.8	
	" 8	10:10 A.M.		−19.8	
		11:00 "	10:40 A.M.	−18.4	
		11:10 "		− 9.2	
		11:20 "		+41.0	June 9 noon
		11:22 "		+ 9.2	
		2:26 P.M.		− 2.6	
	June 10	3:00 "		− 1.6	
	" 14	2:30 "		− 2.1	
L	June 6	1:10 P.M.	12:20 P.M.	− 6.3	
		1:20 "		− 6.3	
		1:30 "		−51.0	
	June 7	1:40 "		−10.5	
		1:55 "		−10.5	
	June 8	10:30 A.M.	8:00 A.M.	−10.5	
	" 10	2:50 P.M.	2:20 P.M.	−54.2	June 11 1:00 P.M.
		2:55 "		−50.4	
	June 14	3:00 "		+ 4.2	no egg
	" 17	2:30 "		− 4.2	" "

The non-ovulatory potential corresponded closely to the potentials of other species (pig, man, goat and dog) and there was a violent rise in potential difference at the time when ovulation must have occurred according to Warren and Scott (1934).[2] Tests were made frequently from the moment when an egg was laid to several hours afterward, and the peak in potential was found forty minutes in one case, twenty-five minutes in another case, and thirty minutes in the third case after oviposition. In both cases the ovum was recovered, that is, both hens laid eggs about 24 hours following their high potential. Two hours after ovulation it had reached normal, non-ovulatory levels.

While these results have to be repeated on a larger scale, it is hoped that some clue will be found as to the direction of the potential in connection with the one-sided ovarian function in the hen. So far, most readings have had negative values, but not all of them.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THERMOSTATIC CONTROL

THE few essential parts required are shown in the accompanying circuit diagram. It will be noticed that no batteries are needed, since the device is completely A.C. operated.

A dual triode tube of the 6A6 type (or equivalent) is employed with the plates and grids connected in parallel. In this circuit the tube acts as a half-wave grid-controlled rectifier. By the use of a bleeder resistor across the A.C. plate supply voltage the grid return through the thermoregulator circuit, TR, may be adjusted to such a value that the grid voltage becomes of sufficient magnitude in phase with the plate voltage to operate the relay, due to the rectified cathode current. The condenser stores sufficient energy and produces enough lag to keep the relay from chattering.

Any sensitive relay that will operate on 15 ma. or less and having from 2,000 to 5,000 ohms may be used. The circuit requires but one preliminary adjustment. Short the input (TR) leads and, starting from point A, move tap P along the bleeder resistance toward B until enough current flows through the relay coil to make it close. To insure reliability it is well to move P a little beyond this point. An alternative method is to merely insert a milliammeter in the plate lead at X and adjust P until the current reads that value specified for the type of relay used.

A "Sigma" type M relay of 2,000 ohms was used in one model of this device. It has been operating a

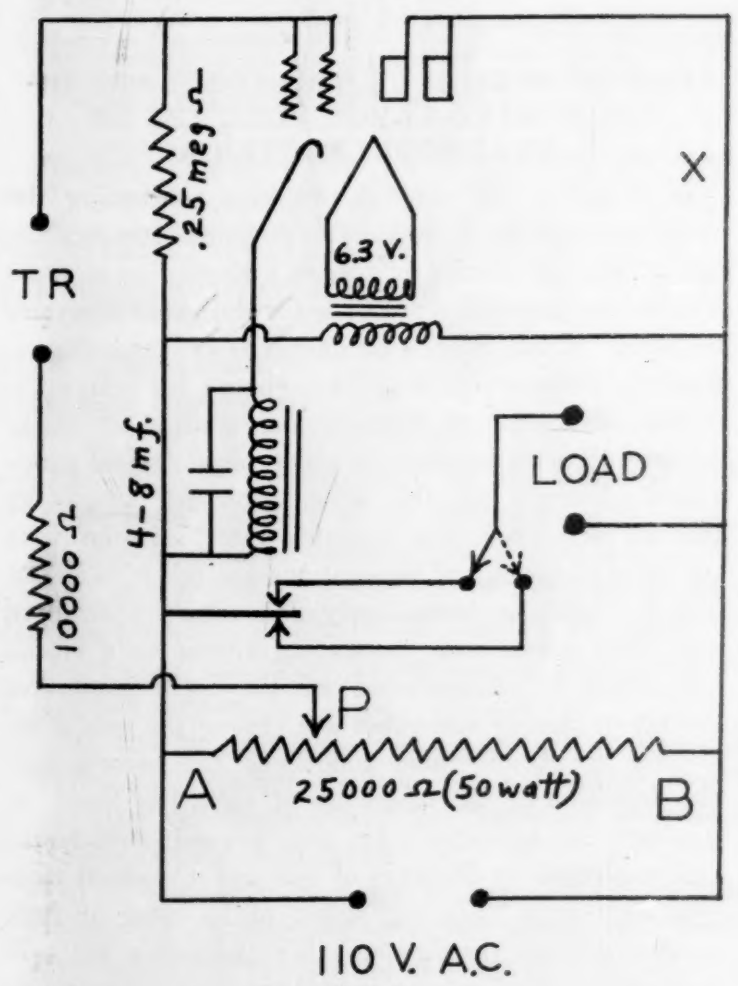

FIG. 1

[2] D. C. Warren and H. M. Scott, SCIENCE, 80: 461–462, 1934.

heating unit in an incubator for over 50 days continuously or more than 1,200 hours without any failure or servicing. This relay is capable of handling up to 500 watts. However, from past experience the writer prefers the use of a mercury type relay switch for control of powers exceeding 300 watts in order to eliminate contact difficulties.

Another model of this device made use of an "Allied" type relay (2,500 ohms). There are many other equally suitable makes available. The control tube operates such relays, whose single pole double throw contacts then operate a power control relay of the mercury tube type.

With either of the two arrangements mentioned the contact combination of the relays allows for either on or off control. The circuit will respond even with poor contact at the input. Grasping one input connection in each hand allows sufficient conductivity to operate the relays.

The complete parts, including the small high resistance control relay, can be secured at a cost of about four dollars. Needless to say the mercury or power control type of relay entails additional expense and determines the successful operation of the device where considerable power is involved.

The choice of thermoregulator to be used with this device is dictated by the sensitivity of control desired.

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USE OF SODIUM THIOGLYCOLLATE IN CULTURING LARGE VOLUMES OF ANAEROBIC BACTERIA

IN many of the present problems concerning the anaerobic bacteria it is desirable to grow large quantities of various strains or species. Examples of these include the production: of cells for antigenic analysis; of toxins of the tetanus or gangrene organisms, particularly when toxoid is to be prepared for active immunization; and of cultures for studies of sugar fermentation mechanisms or other physiological properties. Except for the latter problems, often the medium employed is a complex meat infusion with particles of meat, and precautions are taken to inoculate the medium immediately following sterilization, and other procedures, amounting almost to a ritual, are followed. Since some of the most important disease-producing anaerobes are among the group requiring strict anaerobic conditions for growth any simplification of the technique of culturing these organisms is welcome. In this regard the recent announcement by Brewer[1] of the use of sodium thioglycollate as a reducing agent to be used in fluid media, without vaseline or other protective seals, in the cultivation of anaerobic bacteria is of considerable interest. This compound, a stable salt of thioglycollic acid which may be added to a medium prior to autoclaving, appears to possess advantages over other chemical agents which have been proposed.

We have been interested in the production of cells for antigenic analysis of *Clostridium oedematiens*, which is one of the more strictly anaerobic species in contrast to *Cl. welchii*. The medium used consisted of beef heart infusion broth[2] plus 0.5 per cent. glucose. This medium is autoclaved in 125 cc amounts in 6 oz. oval prescription bottles closed by screw caps. These are inoculated with 2.0 cc of an active meat culture. Successful transplants are possible (and failures with this group are not infrequent) only if the medium is inoculated immediately following autoclaving. With the addition of 0.1 per cent. sodium thioglycollate[3] and 0.01 to 0.05 per cent. agar to this medium we have experienced no failures in several hundred transplants. Further advantage is gained by the fact that the necessity for the immediate inoculation is avoided and the medium, maintaining a reduced state, is satisfactory for those strains which have a prolonged lag phase.

Although our experience has been less extensive with these we have found the thioglycollate of value in culturing strains of *Cl. welchii, Cl. septicum, Cl. oedematoides, Cl. tetani* and *Cl. parabotulinum*. These preliminary results confirm the claims made by Brewer[1] that sodium thioglycollate may have considerable value as a reducing agent, and it is recommended for trial to those engaged in problems which necessitate the culturing of large volumes of anaerobic bacteria. Further studies on specific uses of sodium thioglycollate are in progress and will be reported in later communications together with a consideration of the dehydrated medium also proposed by Brewer.

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[1] J. H. Brewer, *Jour. Bact.*, 39: 10, 1940.

[2] L. S. McClung, *Jour. Bact.*, in press.

[3] Supplied by the Baltimore Biological Laboratories, Baltimore, Maryland.

[4] *Fellow of the John Simon Guggenheim Memorial Foundation.*

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